UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,993	04/04/2002	Pierre Etienne Chabrier de Lassauniere	427.057	5815

20311 7590 06/28/2004

MUSERLIAN AND LUCAS AND MERCANTI, LLP
475 PARK AVENUE SOUTH
NEW YORK, NY 10016

EXAMINER	
ANDERSON, REBECCA L	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 06/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,993	CHABRIER DE LASSAUNIERE ET AL.	
	Examiner	Art Unit	
	Rebecca L Anderson	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,14,15 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,14,15 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/4/02, 4/17/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-6, 14, 15 and 22-25 are currently pending in the instant application and are rejected.

Election/Restrictions

Applicant's election with traverse of the group as now found in the pending claims 1-6, 14, 15 and 22-25 in the reply filed on 29 April 2004 is acknowledged. In the restriction requirement applicant was invited to elect a single invention by identifying another specific embodiment not listed in the groups listed by the Examiner. Applicant has amended the claims to provide this election of another specific embodiment. Applicant traversed the restriction requirement on the ground(s) that the claims have been amended to another specific embodiment, specifically the single invention of the methods of use for the compounds of the formula (I)3. The examiner accepts this amendment as an identification of another specific embodiment not listed in the groups provided by the Examiner in the restriction requirement. Therefore, the instant claims 1-6, 14, 15 and 22-25 will be examined in their entirety.

Claim Objections

Claims 1, 2, 4 and 5 are objected to because of the following informalities:

The objected claims that follow have terms or phrases repeated in the claim.

Claim 1: On page 5, the definition of Q has "is selected from the group consisting of" twice in a row. This should be deleted.

The objected claims that follow have terms and phrases in the claims that apparently should have been deleted from the instant claims. These terms and phrases

are found in areas where every other term has been deleted from the claim, do not define a substituent on the instant formula (I)3, do not make complete statements, i.e. a variable will be stated without a definition and the variable is not on the formula (I)3 or a definition is stated without a variable to define.

Claim 2: Page 19, has the phrase "and T"

Page 21, "aryl", "optionally substituted 1 to 3 times by" and "Ω"

Claim 4: Page 34 "Z3"

Page 35 "(CH2)g-Z4R50", "-(CH2)k-COR51" and "optionally substituted by one"

Claim 5: Page 39 "piperidinyl or N-piperazinyl"

These terms and phrases which are unnecessary and apparently were supposed to be deleted from the claims should be deleted from the claims.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 14, 15 and 22-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the invention is the method of inhibiting monoamine oxidases and lipidic peroxidation and modulating activity vis-a`-vis sodium channels in warm-blooded animals for the treatment of disorders (claims 1-6, 14, 15 and 22), specifically, disorders of the central or peripheral nervous system (claim 23), Parkinson's disease, Alzheimer's disease, Huntington's chlorea, amyotropic lateral sclerosis, peripheral neuropathies (claim 24) and pain (claim 25) with the administration of the compound of formula (I)3 in an effective amount. It is noted that while claims 1-6,14, 15 and 22 do not state "for the treatment of disorders", the claims are drawn to the treatment of disorders since "inhibiting monoamine oxidases", "inhibiting lipid peroxidation" and "having a modulatory effect relative to sodium channels" cannot be considered on their own to be a therapeutic application and once the mechanism of action of a substance has been discovered, it leads to a practical application in the form of an actual treatment for a disorder.

The state of the prior art and the predictablility or lack thereof in the art

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of disorders, whether or not the disease is effected by inhibiting monoamine oxidases and lipidic peroxidation and modulating activity vis-a`-vis sodium channels would make a difference.

It is the state of the art that there is no known cure or prevention for Alzheimer's disease and that there are only four medications available in the United States available to temporarily slow the early stages of Alzheimer's disease. The current drugs for the treatment of Alzheimer's disease, Aricept, Exelon, Reminyl and Cognex, treat early stages of Alzheimer's disease by delaying the breakdown of acetylcholine. Memantine, which blocks excess amounts of glutamate treats late stage Alzheimer's disease.

(URL:http://www.cnn.com/2003/HEALTH/conditions/09/24/alzheimers.drug.ap/index.html).

It is the state of the prior art that autoimmune diseases include acquired immune deficiency syndrom (AIDS) which is the result of an infection with the human immunodeficiency virus (HIV). This virus attacks selected cells of the immune, nervous, and other systems and impairs their proper function. HIV infection may cause damage to the brain and spinal cord via encephalitis (inflammation of the brain) and meningitis (inflammation of the membranes surrounding the brain). It can also cause nerve damage, difficulties in thinking (i.e., AIDS dementia complex), behavioral changes, poor circulation, headache, and stroke. AIDS-related cancers such as lymphoma and opportunistic infections (OI) may also affect the nervous system. Neurological symptoms may be mild in the early stages of AIDS, but can become severe in the final stages. Complications vary widely from one patient to another. Cerebral toxoplasmosis, a common OI in AIDS patients, causes such symptoms as headache, confusion, lethargy, and low-grade fever. Other symptoms may include weakness, speech disturbance, ataxia, apraxia, seizures, and sensory loss. Progressive multifocal leukoencephalopathy (PML), a disorder that can also occur in AIDS patients, causes weakness, hemiparesis or facial weakness, dysphasia, vision loss, and ataxia. Some patients with PML may also develop compromised memory and cognition. There is no cure for AIDS but recently developed treatments help to slow the progression of the disease. Some neurological symptoms and complications may improve with treatment. For example, antidementia drugs may relieve confusion and slow mental decline.

Infections can be treated with antibiotics. Radiation therapy may be needed to treat AIDS-related cancers present in the brain or spinal cord. The overall prognosis for individuals with AIDS in recent years has improved significantly because of new drugs and treatments. AIDS clinicians often fail to recognize neurological complications of AIDS. Those who suspect they are having neurological complications should be sure to discuss these with their doctor. The NINDS supports a broad spectrum of basic and clinical research studies on the neurological complications of AIDS. Much of this research is conducted at leading biomedical research institutions across the country.

(http://www.ninds.nih.gov/health_and_medical/disorders/aids.htm)

Hence, in the absence of a showing of correlation between all the disorders claimed, which includes AIDS, see page 1 the specification, and Alzheimer's disease, as capable of treatment by inhibiting monoamine oxidases and lipidic peroxidation and modulating activity vis-a`-vis sodium channels one of skill in the art is unable to fully predict possible results from the administration of the compound of formula (I)3 due to the unpredictability of the role of the inhibiting monoamine oxidases and lipidic peroxidation and modulating activity vis-a`-vis sodium channels, and since the treatment of Alzheimer's disease is mediated by the breakdown of acetylcholine or the inhibition of excess amounts of glutamate.

The amount of direction or guidance present and the presence or absence of working examples

The only direction and guidance present in the specification is a list of disorders on pages 1, 2 and 69 that applicant considers treatable by inhibiting monoamine

oxidases and lipidic peroxidation and modulating activity vis-a`-vis sodium channels and bond reactions on pages 171-174. There is no correlation between inhibiting monoamine oxidases and lipidic peroxidation and modulating activity vis-a`-vis sodium channels with any disorder let alone Alzheimer's disease or AIDS and the specification does not provide any paharmaceutical data for the treatment of any specific disorder, i.e. the specification is silent and fails to provide guidance as to what diseases are mediated by inhibiting monoamine oxidases and lipidic peroxidation and modulating activity vis-a`-vis sodium channels. There no other guidance or direction present as to what autoimmune diseases can be treated and there is no guidance as to how these other diseases can be treated or prevented.

The breadth of the claims

The breadth of the claims is the method of inhibiting monoamine oxidases and lipidic peroxidation and modulating activity vis-a`-vis sodium channels in warm-blooded animals for the treatment of disorders including AIDS and Alzheimer's disease

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what disorders out of all disorders would be benefited by the inhibiting monoamine oxidases and lipidic peroxidation and modulating activity vis-a`-vis sodium channels and would furthermore then have to determine which of the claimed compounds would provide treatment of the disorder.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the formula (I)3 for inhibiting monoamine oxidases and lipidic peroxidation and modulating activity vis-a`-vis sodium channels in warm-blooded animals for the treatment of disorders by administering the compound of the formula (I)3. As a result necessitating one of skill to perform an exhaustive search for which disorders can be treated by what compounds of formula (I)3 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which disorders can be treated by the compound encompassed in the instant claims, with no assurance of success.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the limitation "in which Het is a heterocycle with 5 members comprising 2 heteroatoms" on page 2. There is insufficient antecedent basis for this limitation in the claim since there is no "Het" to define since applicant has amended the claim to only formula (I)3. Claim 14 recites "wherein Het is formula (I)3 in which". There is insufficient antecedent basis for this limitation in the claim since, again, there is no "Het" the claimed invention has been limited by amendment to the methods using only the formula (I)3. This rejection can be overcome by deleting the statements from the claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 14, 15 and 22-25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of copending Application No. 10/681002. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Applicants instant claims are drawn to the method of inhibiting monoamine oxidases and lipidic peroxidation and modulating activity vis-a`-vis sodium channels in warm blooded animals by administering the compound of the formula (I)3 (claims 1-6, 14, 15 and 22-25. Claims 15 and 22 specify, for example, the compound 2,6-ditert-butyl-4-(4-{2-[methyl(2-propynyl)amino]ethyl}-1,3-oxazol-2-yl)phenol for the compound of the formula (I)3. Claims 23-25 specify certain diseases treated such as the nervous system disease, Parkinson's disease (claims 23 and 24) and pain (claim 25)

Ascertaining the contents of the copending applications claims 1 and 2

Claim 1 of the copending application claims a method of inhibiting lipidic peroxidation and/or inhibiting the monoamine oxydase and/or modulating sodium channels in a patient in need thereof comprising administering to warm-blooded animals the compound of the formula (I)G wherein Het can be, for example, (I)g3, A can be, for example, c) Q substituted phenyl, B can be, for example, hydrogen or alkyl, Y is O or S,

R1 can be, for example, hydrogen, R2 can be, for example hydrogen, n can be an integer from 0 to 6 and Ω is NR46R47 or OR48. Claim 2 of the copending application claims a method of inhibiting lipidic peroxidation and/or inhibiting the monoamine oxydase and/or modulating sodium channels in a patient in need thereof comprising administering to warm-blooded animals the compound of, for example, 2,6-ditert-butyl-4-(4-{2-[methyl(2-propynyl)amino]ethyl}-1,3-oxazol-2-yl)phenol which is within the scope of applicants instant utilized formula (I)3.

The difference between the instant claims and the copending applications claims 1 and 2.

The difference between the instant claims 1-6, 14, 15 and 22 and the copending claim 1 is that the compound utilized in copending claim 1 encompasses the instant compound of the formula (I)3 utilized in the instant invention.

The difference between the instant claims 23-25 and the copending claim 1 is that the compound utilized in the copending claim 1 encompasses the instant compound of the formula (I)3 utilized in the instant invention and the method of claim 1 of the copending application encompasses the specific disorders claimed in applicants instant claims 23-25.

The difference between instant claims 23-25 and copending claim 2 is that while the claim 2 contains the compound, page 267, line 28, 2,6-ditert-butyl-4-(4-{2-[methyl(2-propynyl)amino]ethyl}-1,3-oxazol-2-yl)phenol, which anticipates the instant compound (I)3 utilized in the instant methods, the method of claim 2 encompasses the instant disorders specifically found in the instant claims 23-25.

The difference between claims 1-6, 14, 15 and 22 of the instant application and claim 2 of the copending application is that, while the claims are of varying scope, the copending claim 2 anticpates the instant claims 1-6, 14 and 15 since copending claim 2 claims the method of inhibiting lipidic peroxidation, inhibiting the monoamine oxydase or modulating sodium channels in a patient in need thereof by administering 2,6-ditert-butyl-4-(4-{2-[methyl(2-propynyl)amino]ethyl}-1,3-oxazol-2-yl)phenol9page 267, line 28).

Resolving the level of the skill in the art

Although the instant claims 1-6, 14, 15 and 22-25 differ in scope from those of copending claims 1 and 2. The claims are obvious over the copending claims since claim 2 of copending application claims the method of inhibiting lipidic peroxidation, inhibiting the monoamine oxydase or modulating sodium channels in a patient in need thereof by administering 2,6-ditert-butyl-4-(4-{2-[methyl(2-propynyl)amino]ethyl}-1,3-oxazol-2-yl)phenol9page 267, line 28) which anticipates instant claims 1-6, 14, 15 and 22 and since the copending claim 1 encompasses that which is instantly claimed in claims 1-6, 14, 15 and 22-25 and preferences towards applicants instantly utilized formula (I)3 is found in claim 2 which claims a species of applicants instant formula (I)3, inhibiting lipidic peroxidation, inhibiting the monoamine oxydase or modulating sodium channels in a patient in need thereof by administering 2,6-ditert-butyl-4-(4-{2-[methyl(2-propynyl)amino]ethyl}-1,3-oxazol-2-yl)phenol9page 267, line 28) and preferences towards specific diseases treated is found in the copending specification on page 99, which states that particularly the compounds are useful for treating, for example Parkinson's disease, Alzheimer's disease, Huntington's chorea and pains.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Closest Prior Art

The closest prior art is EP 0908180 which discloses compounds for the treatment of pain which differ from applicants instant compound of the formula (I)3 by applicants substituent Ω. The prior art compound has O-Ar group in the position equivalent to applicants Ω wherein Ar is phenyl or pyridinyl. Applicants Ω, when comprising oxygen, is O-R4 wherein R48 is hydrogen, alkyl, alkynyl or cyanoalkyl.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rebecca Anderson
Patent Examiner
Art Unit 1626, Group 1620
Technology Center 1600

Kamal Saeed
for Joseph McKane
Supervisory Patent Examiner
Art Unit 1626, Group 1620
Technology Center 1600